Complete Summary

GUIDELINE TITLE

National Academy of Clinical Biochemistry and IFCC Committee for standardization of markers of cardiac damage laboratory medicine practice guidelines: Analytical issues for biomarkers of heart failure.

BIBLIOGRAPHIC SOURCE(S)

Apple FS, Wu AH, Jaffe AS, Panteghini M, Christenson RH, Cannon CP, Francis G, Jesse RL, Morrow DA, Newby LK, Storrow AB, Tang WH, Pagani F, Tate J, Ordonez-Llanos J, Mair J, National Academy of Clinical Biochemistry, IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine practice guidelines: Analytical issues for biomarkers of heart failure. Circulation 2007 Jul 31;116(5):e95-8. [30 references] PubMed

Writing Group Members, Apple FS, Wu AH, Jaffe AS, Panteghini M, Christenson RH, NACB Committee Members, Christenson RH, Apple FS, Cannon CP, Frances GS, Jesse RL, Morrow DA, Newby LK, Storrow AB, Tang WH, Wu AH, IFCC Committee on Standardization of Markers of Cardiac Damage (C-SMCD) Members, Apple FS, Cannon CP, Jaffe AS, Pagani F, Tate J, Ordonez-Llanos J, Mair J. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine practice guidelines: analytical issues for biomarkers of heart failure. Clin Biochem 2008 Mar;41(4-5):222-6. [30 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

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METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES
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SCOPE

DISEASE/CONDITION(S)

Heart failure

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Internal Medicine
Pathology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of heart failure
- To address analytical aspects of B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) for clinical use in heart failure

TARGET POPULATION

Patients with suspected or known heart failure

INTERVENTIONS AND PRACTICES CONSIDERED

Characterization of assays for analytical biomarkers (B-type natriuretic peptide [BNP] and N-Terminal proBNP [NT-proBNP]:

- Preanalytical issues (sample type, effect of storage time and temperature)
- Analytical (identification of recognition epitopes, description of calibration material, determination of cross reactivity characteristics, evaluation of dilution response, evaluation of interferences)
- Upper reference limits
- Patients specimen comparisons and regression analyses
- Establishment of receiver operator characteristic (ROC) curves
- Consideration of effects of ethnicity

MAJOR OUTCOMES CONSIDERED

Clinical effectiveness (sensitivity and specificity) and prognostic/therapeutic utility of clinical biomarker testing in heart failure

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

These National Academy of Clinical Biochemistry (NACB) guidelines were developed rigorously; however it was possible to include only papers published in the English language. The specified method for developing the evidence base for recommendations listed involved use of PubMed, EMBASE, and other databases that were not necessarily published. Systematic methods were used whenever available; searches were first set to be sensitive to avoid missing papers of possible interest, and then narrowed to sort through the literature in order to enhance specificity. The writing group contacted recognized experts to assure that important evidence had not been missed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

B - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

C - Expert Consensus was the primary basis for the recommendation

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Academy of Clinical Biochemistry's (NACB) Laboratory Medicine Practice Guidelines (LMPG) for use of cardiac markers in coronary artery diseases were published in July of 1999. Since production of this initial document, numerous published studies and presented data have added significantly to the knowledge base for cardiac biomarkers. This increased knowledge has substantially expanded the scope of recommendations for cardiac biomarker utilization since the 1999 document, and in particular has required the inclusion of recommendations regarding biomarkers that extend beyond myocardial necrosis. Toward addressing these advances and their impact on biomarker utilization in clinical practice, the NACB appointed a chair and members of a LMPG committee that was charged with the overall objective of revising and extending the earlier recommendations by establishing modern guidelines for Utilization of Biomarkers in Acute Coronary Syndrome and Heart Failure. This LMPG is aimed at providing analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS), heart failure and point-of-care measurement and logistics of providing ACS biomarker data for patient care; guidance for interpretation of biomarkers in etiologies other than ACS and Heart Failure is included as well.

These guidelines and their recommendations are structured into six chapters that include Chapter 1: Clinical Utilization of Biomarkers in Acute Coronary Syndromes (ACS); Chapter 2: Analytical Issues of ACS Biomarkers; Chapter 3: Clinical Utilization of Biomarkers of Heart Failure; Chapter 4: Analytical Issues of Heart Failure Biomarkers; Chapter 5: Point of Care Testing and Logistics; and Chapter 6: Cardiac Biomarkers and Other Etiologies. Each chapter was spearheaded by a writing group, which was a subset of the overall committee. In addition, other ad hoc expertise contributed to the writing group of some subsections and chapters

to optimize the content and quality of the guidelines. The "questions" for each chapter are in the form of issues addressed and specified in the organization of each individual chapter. The chapter design of the guidelines was used to facilitate finding guidance by users; this format was also used, in part, to provide an easy and focused procedure for updating the guidelines in the future. Also, the chapter design allowed publication of sections in appropriate laboratory medicine and clinical specialty journals.

Stakeholder involvement in development and refinement of these guidelines was substantial. The guideline team was comprised of laboratory medicine, ACS cardiology experts, and heart failure cardiology experts. As these guidelines target acutely ill patients, Emergency Medicine stakeholders were represented by a specialist; it is also noteworthy that all of the laboratory professionals and cardiology experts on the guideline committee have substantial interaction, knowledge, and publications in the area of laboratory and clinical medicine in the Emergency Medicine environment.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Modified American College of Cardiology/American Heart Association Classifications: Summary of Indications

Class I: Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or treatment.

> **Class IIa**: Weight of evidence/opinion is in favor of usefulness/efficacy.
>
> **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Stakeholder involvement in development and refinement of these guidelines was substantial. To further enhance stakeholder input, draft revisions of the Guidelines

were prepared and placed for comment on the National Academy of Clinical Biochemistry (NACB) World Wide Web site (http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/DraftGuidelines/BioHearFailure/). The draft Laboratory Medicine Practice Guidelines (LMPG) and suggested revisions were also presented for public and stakeholder comment at the October 2004 Arnold O. Beckman Conference titled *Cardiac Markers: Establishing Guidelines and Improving Results*. Refer to Table 1 of the Preamble to the original guideline document for a list of the various stakeholder groups that agreed to examine the documents and were represented at the conference.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the weight of evidence (A-C) and the summary of indications (Classes I, II, IIa, IIb, III) are presented at the end of the "Major Recommendations" field.

Note from the National Academy of Clinical Biochemistry (NACB) and the National Guideline Clearinghouse (NGC)*: The Laboratory Medicine Practice Guidelines (LMPG) for utilization of biochemical markers in acute coronary syndromes and heart failure* have been divided into individual summaries. In addition to the current summary, the following are available:

- Chapter 1: Clinical characteristics and utilization of biochemical markers in acute coronary syndromes
- Chapter 2: Analytical issues for biochemical markers of acute coronary syndromes
- Chapter 3: Clinical utilization of cardiac biomarker testing in heart failure
- Chapter 5: Point of care testing, oversight and administration of cardiac biomarkers for acute coronary syndromes
- Chapter 6: Use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure

Analytical Biomarker Issues

Issues Related to B-type Natriuretic Peptide (BNP) and N-Terminal pro-BNP Natural Peptide (NT-proBNP) Measurement

Recommendations for analysis of biochemical markers of heart failure

Class I

1. Before introduction into clinical practice, BNP and NT-proBNP assays must be characterized with respect to the following preanalytical and analytical issues.

   Preanalytical:

   a. Sample type; including type of biological sample: serum, plasma, whole blood; and type of specimen collection tubes

b. Effect of storage time and temperature

Analytical:

a. Identification of antibody recognition epitopes
b. Description of calibration material used; with identification of source and the concentration value assignment. Until a clear determination of the clinically relevant molecules is established and a corresponding reference system is defined, results for both BNP and NT-proBNP should be reported in micrograms/L, rather than pmol/L.
c. Determination of cross reactivity characteristics with related natriuretic peptides (NPs), especially for BNP, NT-proBNP and proBNP, as well as for, atrial natriuretic peptide, NT-proANP, C-type natriuretic peptide
d. Evaluation of dilution response
e. Evaluation of interferences such as heterophile antibodies, rheumatoid factors, human antimouse antibodies **(Level of Evidence: C)**

2. Upper reference limits, at the 97.5th percentile of the reference value distribution, should be independently established for both BNP and NT-proBNP based on age, by decade, and by gender. Each commercial assay should be validated separately. **(Level of Evidence: C)**
3. Patients specimen comparisons and regression analysis should be performed, along Clinical and Laboratory Standards Institute (CLSI) (formerly the National Committee for Clinical Laboratory Standards [NCCLS]) guidelines, to establish the degree of or lack of harmonization across the dynamic range of each assay. Harmonization has been proposed around the current presumed optimal diagnostic medical decision cutoff for heart failure of 100 micrograms/L for BNP, as found in the Breathing Not Properly Trial using the Biosite assay (Maisel et al., 2002). This may not be ideal for other nonheart failure clinical situations. More formal harmonization efforts might well be necessary along the lines done for other analytes, i.e., cardiac troponin and creatine kinase MB. Since there is only one source of antibodies and calibrators for NT-proBNP (Roche), harmonization of NT-proBNP assays should not be a problem. **(Level of Evidence: C)**
4. Receiver operating characteristic (ROC) curves should be established to evaluate the clinical effectiveness and to establish optimal medical decision cutoffs for both BNP and NT-proBNP assays for diagnostic usefulness. Data need to be reported in concentration numbers to allow for consensus between assays and not only in quartiles and tertiles. **(Level of Evidence: C)**

Class IIa

1. Assays for BNP and NT-proBNP should have a total imprecision (% coefficient of variation [CV]) of <15% at concentrations corresponding to their age and gender defined upper reference limits. **(Level of Evidence: C)**
2. The effect of ethnicity needs to be evaluated as a possible independent variable. **(Level of Evidence: C)**
3. Caution should be exercised in interpreting <50% concentration changes as being related to medical therapy because a consistently high biological variation for both BNP and NT-proBNP exists. However, consistent trends should be followed as clinically important. **(Level of Evidence: B)**

Definitions:

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

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C - Expert Consensus was the primary basis for the recommendation

Summary of Indications

Class I: Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

This guideline may help establish uniform criteria so that the analytical qualities and clinical performance of assays natriuretic peptide and their related co-metabolites can be evaluated objectively.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The materials in this publication represent the opinions of the authors and committee members, and do not necessarily represent the official position of the National Academy of Clinical Biochemistry (NACB) or the International Federation of Clinical Chemistry (IFCC). The National Academy of Clinical Biochemistry is the academy of the American Association for Clinical Chemistry.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Apple FS, Wu AH, Jaffe AS, Panteghini M, Christenson RH, Cannon CP, Francis G, Jesse RL, Morrow DA, Newby LK, Storrow AB, Tang WH, Pagani F, Tate J, Ordonez-Llanos J, Mair J, National Academy of Clinical Biochemistry, IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine practice guidelines: Analytical issues for biomarkers of heart failure. Circulation 2007 Jul 31;116(5):e95-8. [30 references] PubMed

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Jul (revised 2007 Jul)

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

GUIDELINE COMMITTEE

The National Academy of Clinical Biochemistry

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Other than modest funding from the National Academy of Clinical Biochemistry/American Association for Clinical Chemistry (NACB/AACC), development of these guidelines was a volunteer activity. Thus the guidelines are editorially independent from any funding body.

All potential conflicts of interest for the NACB guidelines committee and ad hoc members of the writing committees are listed at the following: http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/PublishedGuidelines/ACSHeart/heartpdf.htm.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Preamble. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for utilization of biochemical markers in acute coronary syndromes and heart failure. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2007. p. 1-3.

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 12, 2008. The information was verified by the guideline developer on April 2, 2008.

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